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ARTIFICIAL HIBERNATION IN THE WOODCHUCK (ARCTOMYS MONAX)

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The phenomenon of hibernation in the mammal is of interest, presenting, as it does, peculiar problems in heat regulation and metabolism. The transition from the homoiothermic to the poikilothermic state and the associated nutritional changes have been the subject of considerable research. Since much of the previous evidence seemed to indicate the existence of a close relationship between the mechanism of hibernation and the blood sugar level, the authors (1925) reported the results of experiments in which the combined effects of lowered body temperature and of insulin hypoglycemia were investigated. Inasmuch as animals that hibernate naturally were not obtainable at the time, dogs and cats were used. It was found that even in these animals a state simulating hibernation could be induced. The dogs and cats were anesthetized with amytal, cooled by immersion in a cold bath, and then given insulin. Two to four hours later, when the blood sugar concentration had fallen to 45 mgm. per cent (*circ.*), the animals ceased to shiver even though their body temperature was about 13°C. below the normal. The condition of the animals at this time was such as to suggest an analogy to the hibernating state particularly in the following respects: 1, the tendency of the animal to assume the temperature of its surroundings; 2, the absence of shivering and of spontaneous movements; 3, the loss of consciousness; 4, the profound reduction in the rate of metabolism; and 5, a prolonged state of hypoglycemia without convulsions. Since it appeared that the capacity for shivering was of prime importance as regards the recovery of normal temperature, and since this in turn had been found to depend upon the concentration of the blood sugar, it was concluded that insulin was related to the mechanism of hibernation. The results of similar experiments on an hibernating species are reported in the present communication.

American woodchucks (*Arctomys monax*) were used in this research. These animals were trapped during the month of May, and for a month

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preceding the experiments were kept in large wire cages, their food consisting for the most part of green vegetables, potatoes, and carrots. At the time of use the animals were all healthy and active. In the earlier experiments the method of procedure was the same as that described in our previous paper (1925). The protocol of one of these experiments follows:

Woodchuck 1. Weight 1.51 kgm.

10:51 Given 0.5 cc. of 10 per cent sodium amytal solution per kilogram intraperitoneally. Body temperature 38.7°C.
11:25 Immersed in a cold bath. Vigorous shivering
11:40 Body temperature 22.5°C. Removed from bath
12:00 Body temperature 20°C. Blood sugar 116 mgm. per cent
12:05 Given 3 units insulin per kilogram. Shivering vigorously
12:25 Body temperature 24°C. Animal wetted
12:50 Body temperature 23.3°C. Shivering vigorously
2:50 Body temperature 24°C. Shivering vigorously
3:15 Body temperature 25.1°C. Shivering vigorously
3:40 Blood sugar 56 mgm. per cent.
4:15 Body temperature 26°C. Animal given 3 units insulin per kilogram
4:25 Body temperature 27°C. Immersed in cold bath
4:31 Body temperature 22.6°C. Removed from bath
4:45 Body temperature 19.7°C. Animal still shivering
5:26 Blood sugar 67 mgm. per cent. Given 3 units insulin per kilogram
6:20 Body temperature 21.7°C. Shivering vigorously
7:30 Blood sugar 51 mgm. per cent. Given 5 units insulin per kilogram
8:30 Body temperature 25°C. Shivering vigorously
8:35 Given 5 units insulin per kilogram. Immersed in cold bath
8:45 Body temperature 23.5°C. Removed from bath. Shivering vigorously
11:00 Body temperature 25.5°C. Blood sugar 44 mgm. per cent. Shivering vigorously. Animal killed

In the above experiment shivering was not abolished at any time, and the temperature of the animal tended to rise whenever it was below normal. It was inferred that this was due to the fact that the blood sugar concentration did not at any time fall to a sufficiently low level to abolish shivering, even though large amounts of insulin had been injected. In order to produce a more profound hypoglycemia, another woodchuck was given insulin before immersion in the cold water; for, as has long been known, the emotional stimulation caused by the sudden exposure of an animal to cold produces a rise in the blood sugar concentration. The details of this experiment are given below:

Woodchuck 2. Weight 1.55 kgm.

June 21
10:45 Given 0.5 cc. of 10 per cent sodium amytal solution per kilogram
11:05 Given 0.1 cc. amytal per kilogram
11:30 Given 0.1 cc. amytal per kilogram
11:50 Body temperature 38°C. Blood sugar 161 mgm. per cent

12:00 Given 5 units of insulin per kilogram subcutaneously
4:00 Blood sugar 44 mgm. per cent
4:05 Given 5 units of insulin per kilogram subcutaneously
6:55 Animal completely relaxed
7:10 Body temperature 37°C. Blood sugar 36 mgm. per cent
8:18 Body temperature 37°C. Feeble tonic convulsion
8:30 Immersed in cold bath. No shivering
8:40 Slight shivering. Removed from bath. Blood sugar 97 mgm. per cent
8:45 Immersed in bath
9:07 Removed from bath. Slight shivering. Body temperature 22°C.
9:28 Body temperature 21.5°C.
10:55 Body temperature 18°C. Shivering vigorously
11:25 Blood sugar 70 mgm. per cent. Given 5 units of insulin per kilogram subcutaneously

June 22

12:15 Body temperature 26°C. Shivering vigorously. Immersed in bath
12:27 Body temperature 20.8°C. Shivering vigorously. Removed from bath
12:50 Body temperature 20.3°C. Shivering vigorously
1:40 Body temperature 26.5°C. Shivering vigorously. Given 10 units of insulin per kilogram
9:50 Animal in a state of profound torpidity, lying partly turned on its back with limbs outstretched. Body temperature 24°C. Temperature of room 23°C.
10:54 Body temperature 24°C. Blood sugar 19 mgm. per cent
2:12 Body temperature 25°C. Temperature of room 23.5°C.
4:36 Body temperature 25.5°C. Temperature of room 23.4°C.
9:30 Body temperature 25.7°C. Temperature of room 23.5°C.

June 23

9:00 Body temperature 30°C. Temperature of room 24°C. Blood sugar 59 mgm. per cent. Animal semi-torpid and capable of slow movement, if stimulated. Wetted with cold water. No shivering
9:10 Given 5 units of insulin per kilogram
11:15 Body temperature 21.5°C.
5:21 Body temperature 22.5°C. Blood sugar 60 mgm. per cent. Feeble movements and slight shivering. Animal died during removal of sample

The blood sugar concentration of this woodchuck fell to 36 mgm. per cent 7 hours and 10 minutes after the first administration of 5 units of insulin per kilogram. When the animal was immersed in a cold bath, no shivering was observed until 10 minutes had elapsed. At the moment when shivering was first noticed, the blood sugar had risen to 97 mgm. per cent. This indicates that hypoglycemia abolishes shivering in the woodchuck, but that immersion of an hypoglycemic woodchuck in cold water causes a marked increase in the blood sugar concentration, and this is followed by shivering. As previously pointed out by the authors (1926a) the domestic fowl behaves similarly.

Once the body temperature of the woodchuck had been lowered, and profound hypoglycemia induced by means of repeated injections of insulin, the animal passed into a state of artificial hibernation. Before assuming this state of torpidity, the woodchuck was shivering vigorously,

and its temperature rose from 20.3°C. to 26.5°C. in 50 minutes. Several hours later, when the blood sugar had fallen to 19 mgm. per cent and shivering had disappeared, the animal's temperature fell to 24°C. and remained at approximately this level for 12 hours, the surrounding temperature varying during this period from 23°C. to 23.5°C. The following morning (June 23) the temperature of the animal had risen to 30°C., and the woodchuck was in a semi-torpid condition; *i.e.*, stimulation evoked slow body movements. It was found that the blood sugar concentration had increased to 59 mgm. per cent. The woodchuck was wetted with cold water, and given an additional 5 units of insulin per kilogram. Its temperature fell rapidly to 21.5°C., and the animal once more became completely torpid. However, the tendency of the blood sugar level to rise was still marked; for, in spite of the insulin administration, the blood contained 60 mgm. per cent of sugar at 5:21 p.m. At this time the animal began to shiver and move about, although its temperature had risen only 1°C.

From the above it became apparent that it would be necessary to administer insulin at intervals in order to keep these animals in a state of torpidity for a considerable period of time. In order to simulate more closely natural conditions, it was decided to give insulin to woodchucks and then to place them in a cool chamber. This procedure made the use of amytal unnecessary, and, in addition, eliminated the excessive stimulation caused by immersion in cold water. It was also possible to keep the animals completely dry, so that evaporation of water would not be a factor in lowering their body temperature. The cooling chamber was the same as that used by Tait and Britton (1923) in a series of experiments on the artificially cooled woodchuck. It was a large, felt-covered, double-walled chamber with a glass window through which the animal could be observed. The space between the walls was filled with ice. The animals were placed in a wire cage within the chamber, to prevent them from coming into contact with the cold walls.

As a control experiment, a woodchuck without insulin was placed in the cooling chamber for a period of 8 hours. It was able to maintain a body temperature of 37.3°C. without shivering or moving about to any considerable extent. The temperature of the chamber varied from 6°C. to 13°C. The animal was then given 30 units of insulin per kilogram. The following morning this woodchuck was partially torpid and a few hours later was completely dormant. Its temperature at this time was 28°C.

Another woodchuck was given insulin (25 units per kilogram), at 3 p.m. on June 24. At 6 p.m. the animal was inactive, and at 10:15 p.m. semi-torpid. On the morning of June 25 the animal was in a state of profound

torpor, its temperature having fallen to 12.1°C. The temperature of the chamber was 11°C. At 8:30 that evening the temperature of the chamber had risen to 16.5°C. and the temperature of the animal was 17.8°C. The woodchuck was given a second injection of insulin. The next morning (June 26) it was still completely torpid in spite of the fact that its temperature had risen to 28°C. At this time the temperature within the chamber was 22.5°C. The chamber was repacked with ice. At 10:05 p.m. the temperature within the chamber had fallen to 11°C. and that of the animal to 10°C. The woodchuck was completely dormant and even

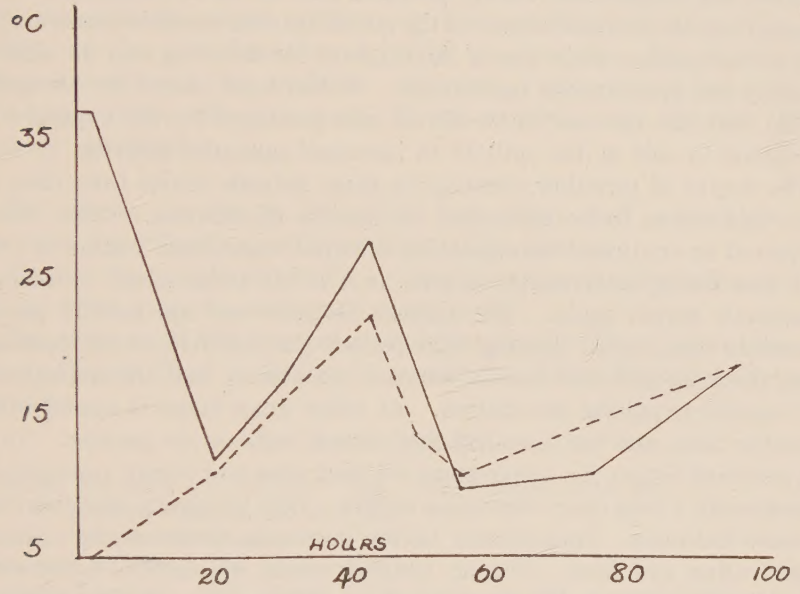

Fig. 1. Curves showing the relation of the temperature of an hypoglycemic woodchuck to that of its environment. Continuous line—temperature of animal. Broken line—temperature of environment.

the corneal reflex was absent. The next evening (June 27) the animal's temperature was 11.3°C. that of the chamber being 15°C. The animal received a third injection of insulin (10 units per kilogram). On the afternoon of June 28 this woodchuck was still asleep. The temperature of the animal was the same as that of the chamber—19°C. The relation of the temperature of this animal to that of its environment is shown in figure 1. At 3:18 p.m. this animal received 2 cc. of adrenalin (1:1000 solution) subcutaneously, in order to increase the blood sugar concentration and thus cause the animal to shiver (the authors, 1926b). Fifteen minutes after the injection there was a marked increase in the rate and

depth of respiration. Six minutes later the woodchuck began to shiver and to move about. Unfortunately the animal died during an attempt to obtain a sample of blood from the heart. A similar experiment was carried out on an amytalized woodchuck. This animal remained dormant for $2\frac{1}{2}$ days at the end of which time it died.

Tait and Britton (1923) found that woodchucks recovered their normal temperature spontaneously and promptly after having been cooled artificially to temperatures varying between 12°C. and 3°C. As has been described above, a woodchuck with hypoglycemia becomes poikilothermic; its temperature closely parallels that of its surroundings. The change from the homoiothermic to the poikilothermic condition is undoubtedly a consequence of the loss of the capacity for shivering and the ability to carry out spontaneous movements. It has been shown by Morgulis (1924) that the increase in metabolic rate produced by the exposure of an animal to cold is due entirely to increased muscular activity.

The degree of torpidity observed in these animals varies from time to time, and seems to be influenced by outside stimulation. Often when subjected to continued manipulation a torpid woodchuck begins to execute slow feeble movements; as soon as it is left undisturbed, it becomes completely torpid again. The animals lie inert and are usually partly turned on their back. During some periods there is little or no muscular tone, the knee-jerk and corneal reflexes are absent, and the animals do not respond to painful stimulation. At other times there is considerable muscular tone, and the knee-jerk and corneal reflexes are present. During profound torpor the respirations are very slow and barely perceptible. Occasionally a long deep respiration occurs. Biot breathing was observed in some instances. Immediately before becoming dormant the animals passed urine and feces. During torpidity small amounts of urine were occasionally voided. Whereas insulin convulsions may be produced readily in woodchucks at normal body temperature, no convulsions were observed in these animals when their body temperature had been lowered. Hence, lowered body temperature inhibits insulin convulsions in woodchucks as it does in dogs and cats.

The authors (1925) have shown that administration of glucose to a cooled hypoglycemic dog or cat causes the shivering reflex to reappear, and as a result the animal regains its normal condition. Two grams per kilogram of glucose in 20 per cent solution were injected into a woodchuck after artificial hibernation had been induced. Shivering began 4 minutes later and became vigorous within 8 minutes. Sixteen minutes after receiving the sugar, the animal was actively moving about and interested in its surroundings. Within 4 hours its temperature had risen to 36.5°C., and the woodchuck was entirely normal.

SUMMARY

When a woodchuck is given an amount of insulin sufficient to produce profound hypoglycemia, it loses its power of temperature control. If it then be placed in an environment even moderately cool, it passes into a state of artificial hibernation. The characteristics presented by an animal in this condition are: 1, the woodchuck becomes poikilothermic; 2, it is unable to shiver or execute spontaneous movements; 3, consciousnes is lost, and the animal is insensible to painful stimulation; 4, the convulsions associated with insulin hypoglycemia do not occur; 5, the metabolic rate is greatly decreased. The state of torpor thus induced can be prolonged by the administration of insulin at intervals. The injection of glucose terminates this condition. Shivering begins almost immediately, the temperature rises at a rapid, though variable, rate, and the animal returns to normal.

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